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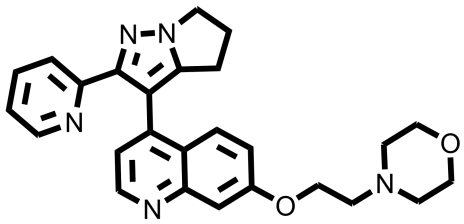
TGFβ Inhibitor LY2109761

Chemical Name: 4-(2-((4-(2-(pyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl)quinolin-7-yl)oxy)ethyl)morpholine



Molecular Weight:	441.52
Formula:	$C_{26}H_{27}N_5O_2$
Purity:	≥98%
CAS#:	700874-71-1
Solubility:	DMSO up to 100mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

LY2109761 is a highly potent and selective TGFβ receptor type I and type II (TβRI/II) inhibitor with Ki of 38 nM and 300 nM respectively. Blocking TβRI/II kinase activity with LY2109761 completely suppresses both the basal and TGF-β1-stimulated migration and invasion of L3.6pl/GLT cells, and completely suppresses TGF-β–induced Smad2 phosphorylation. LY2109761 treatment at 1 nM is sufficient to significantly block the migration and invasion but not adhesion of hepatocellular carcinoma cells by increasing E-cadherin expression. It can also reduce the self-renewal and proliferation of GBM-derived cancer stem–like cells, which can be significantly enhanced when combined with radiation. Administration of LY2109761 alone or in combination with gemcitabine or with radiation demonstrated very good efficacy in multiple xenograft mice models.

How to Use:

In vitro: LY2109761 was usually used at 5-10 μM in vitro and in cellular assays.

In vivo: LY2109761 was orally dosed to mice at 50 mg/kg once per day or in combination with gemcitabine (25 mg/kg) to significantly reduce the tumor volume.

Reference:

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2. Melisi D, et al. LY2109761, a novel transforming growth factor beta receptor type I and type II dual inhibitor, as a therapeutic approach to suppressing pancreatic cancer metastasis. (2008) Mol Cancer Ther. 7(4):829-40.
3. Zhang B, et al. Targeting transforming growth factor-beta signaling in liver metastasis of colon cancer. (2009) Cancer Lett. 277(1):114-20.
4. Connolly EC, et al. Outgrowth of drug-resistant carcinomas expressing markers of tumor aggression after long-term TβRI/II kinase inhibition with LY2109761. (2011) Cancer Res. 71(6):2339-49.
5. Zhang M, et al. Blockade of TGF-β signaling by the TGFβR-I kinase inhibitor LY2109761 enhances radiation response and prolongs survival in glioblastoma. (2011) Cancer Res. 71(23):7155-67.
6. Flechsig P, et al. LY2109761 Attenuates Radiation-Induced Pulmonary Murine Fibrosis via Reversal of TGF-β and BMP-Associated Proinflammatory and Proangiogenic Signals. (2012) Clin Cancer Res. 18(13):3616-27